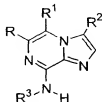


CLAIMS

What is claimed is:

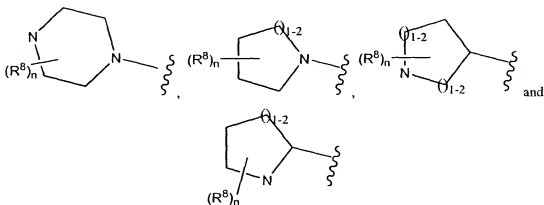
1. A compound represented by the structural formula



Formula III

wherein:

R is selected from the group consisting of alkyl, CF₃, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, arylalkyl, -C(O)R⁷,

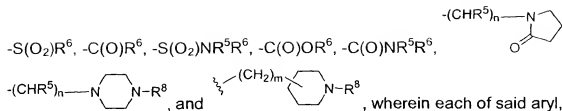


wherein each of said alkyl, heteroaryl, arylalkyl, cycloalkyl, heterocyclyl and the heterocyclyl moieties whose structures are shown immediately above for R can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, cycloalkyl, CF₃, CN, -OCF₃, -OR⁶, -C(O)R⁷, -NR⁵R⁶, -C(O₂)R⁶, -C(O)NR⁵R⁶, -(CHR⁵)_nOR⁶, -SR⁶, -S(O₂)R⁷, -S(O₂)NR⁵R⁶, -N(R⁵)S(O₂)R⁷, -N(R⁵)C(O)R⁷ and -N(R⁵)C(O)NR⁵R⁶;

R¹ is H, halogen or alkyl;

R² is selected from the group consisting of H, halogen, CN, cycloalkyl, heterocyclyl, alkynyl and -CF₃;

R³ is selected from the group consisting of aryl (with the exception of phenyl), heteroaryl (with the exception of furyl), heterocyclyl, -(CHR⁵)_n-heteroaryl,



heteroaryl and heterocyclyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being

- 5 independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF₃, CN, -OCF₃, -OR⁵, -NR⁵R⁶, -C(O₂)R⁵, -C(O)NR⁵R⁶, -SR⁶, -S(O₂)R⁶, -S(O₂)NR⁵R⁶, -N(R⁵)S(O₂)R⁷, -N(R⁵)C(O)R⁷ and -N(R⁵)C(O)NR⁵R⁶, with the proviso that when R³ is -(CHR⁵)_n-heteroaryl, R² can additionally be alkyl;

R⁵ is H or alkyl;

- 10 R⁶ is selected from the group consisting of H, alkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl, wherein each of said alkyl, heteroarylalkyl, aryl, heteroaryl and arylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF₃, OCF₃, CN, -OR⁵, -NR⁵R⁶, -CH₂OR⁵, -C(O₂)R⁵, -C(O)NR⁵R⁶, -SR⁶, -S(O₂)R⁷, -S(O₂)NR⁵R⁶, -N(R⁵)S(O₂)R⁷, -N(R⁵)C(O)R⁷ and -N(R⁵)C(O)NR⁵R⁶;

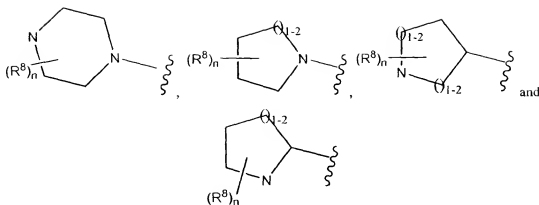
- 15 R⁷ is selected from the group consisting of alkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl, wherein each of said alkyl, heteroarylalkyl, aryl, heteroaryl and arylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF₃, OCF₃, CN, -OR⁵, -NR⁵R⁶, -CH₂OR⁵, -C(O₂)R⁵, -C(O)NR⁵R⁶, -SR⁶, -S(O₂)R⁷, -S(O₂)NR⁵R⁶, -N(R⁵)S(O₂)R⁷, -N(R⁵)C(O)R⁷ and -N(R⁵)C(O)NR⁵R⁶;

- 20 R⁸ is selected from the group consisting of R⁶, -C(O)NR⁵R⁶, -S(O₂)NR⁵R⁶, -C(O)R⁷, -C(O₂)R⁶, -S(O₂)R⁷ and -(CH₂)-aryl;

m is 0 to 4; and

n is 1-4.

- 25 2. R is selected from the group consisting of alkyl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, arylalkyl,


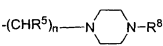



wherein each of said alkyl, heteroaryl, cycloalkyl, arylalkyl, heterocyclyl and the heterocyclyl moieties shown above for R can be unsubstituted or optionally

- 5 independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, cycloalkyl, CF_3 , CN, $-\text{OCF}_3$, $-\text{OR}^6$, $-\text{C(O)R}^7$, $-\text{NR}^5\text{R}^6$, $-\text{C(O}_2)\text{R}^6$, $-\text{C(O)NR}^5\text{R}^6$, $-\text{SR}^6$, $-\text{S(O}_2)\text{R}^7$, $-\text{S(O}_2)\text{NR}^5\text{R}^6$, $-\text{N(R}^5)\text{S(O}_2)\text{R}^7$, $-\text{N(R}^5)\text{C(O)R}^7$ and $-\text{N(R}^5)\text{C(O)NR}^5\text{R}^6$.

- 10 R^1 is H or halogen;

R^2 is selected from the group consisting of H, halogen, cycloalkyl, CN, alkynyl and $-\text{CF}_3$;

R^3 is selected from the group consisting of aryl, heteroaryl, heterocyclyl, $-(\text{CHR}^5)_n$ -heteroaryl, $-\text{S(O}_2)\text{R}^6$, $-\text{C(O)R}^6$, $-\text{S(O}_2)\text{NR}^5\text{R}^6$, $-\text{C(O)OR}^6$, $-\text{C(O)NR}^5\text{R}^6$, $-(\text{CHR}^5)_n$ -, $-(\text{CHR}^5)_n$ -, $-(\text{CH}_2)_m$ -, wherein each of

- 15 said aryl, heteroaryl and heterocyclyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF_3 , CN, $-\text{OCF}_3$, $-\text{N(R}^5)\text{C(O)R}^7$, $-\text{C(O)NR}^5\text{R}^6$, $-\text{S(O}_2)\text{R}^6$, and $-\text{N(R}^5)\text{C(O)R}^7$;

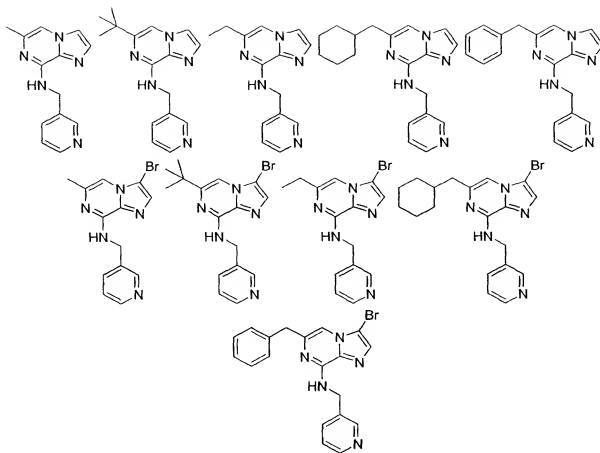
R^5 is H or lower alkyl;

m is 0 to 2; and

n is 1 to 3.

3. The compound of claim 2, wherein R is alkyl, arylalkyl or cycloalkylalkyl.

4. The compound of claim 3, wherein R is selected from the group consisting of methyl, ethyl, t-butyl, cyclohexylmethyl, benzyl and phenethyl.
5. The compound of claim 2, wherein R¹ is H.
6. The compound of claim 2, wherein R¹ is methyl.
- 5 7. The compound of claim 2, wherein R² is H, F, Cl, Br or I.
8. The compound of claim 7, wherein R² is Br.
9. The compound of claim 8, wherein R³ is (pyrid-2-yl)methyl, (pyrid-3-yl)methyl, (pyrid-4-yl)methyl, thien-2-yl or thien-3-yl, wherein said pyridyl and thienyl can be unsubstituted or optionally independently substituted with one or more
10 moieties which can be the same or different, each moiety being independently selected from the group consisting of F, Cl, Br, CF₃, lower alkyl, methoxy and CN.
10. The compound of claim 9, wherein R³ is (pyrid-2-yl)methyl.
11. The compound of claim 9, wherein R³ is (pyrid-3-yl)methyl.
12. The compound of claim 9, wherein R³ is (pyrid-4-yl)methyl.
- 15 13. The compound of claim 2, wherein m is 0.
14. The compound of claim 2, wherein n is 1.
15. A compound of the formula:



- 5 or a pharmaceutically acceptable salt or solvate thereof.
16. A method of inhibiting one or more cyclin dependent kinases, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such inhibition.
17. A method of treating one or more diseases associated with cyclin
- 10 dependent kinase, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such treatment.
18. The method of claim 17, wherein said cyclin dependent kinase is CDK2.
19. The method of claim 17, wherein said cyclin dependent kinase is mitogen activated protein kinase (MAPK/ERK).
- 15 20. The method of claim 17, wherein said cyclin dependent kinase is glycogen synthase kinase 3 (GSK3beta).
21. The method of claim 17, wherein said disease is selected from the group consisting of:

cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma;

leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma;

acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia;

fibrosarcoma, rhabdomyosarcoma;

astrocytoma, neuroblastoma, glioma and schwannomas; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratocanthoma, thyroid follicular cancer and Kaposi's sarcoma.

22. A method of treating one or more diseases associated with cyclin dependent kinase, comprising administering to a mammal in need of such treatment

an amount of a first compound, which is a compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof; and

an amount of at least one second compound, said second compound being an anti-cancer agent;

wherein the amounts of the first compound and said second compound result in a therapeutic effect.

23. The method of claim 22, further comprising radiation therapy.

24. The method of claim 22, wherein said anti-cancer agent is selected from the group consisting of a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chlormethine, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine,

- 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, oxaliplatin, leucovorin, ELOXATIN™, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Teniposide 17 α -Ethinylestradiol,
- 5 Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin,
- 10 Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrozole, Letrozole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.
25. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 1 in combination with at least one
- 15 pharmaceutically acceptable carrier.
26. The pharmaceutical composition of claim 25, additionally comprising one or more anti-cancer agents selected from the group consisting of a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil,
- 20 methotrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chlormethine, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin,
- 25 Dacarbazine, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Teniposide 17 α -Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone,
- 30 Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine,

Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrozole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.

- 5 27. A compound of claim 1 in purified form.